

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing (day/month/year) 11 OCT 2005	
FOR FURTHER ACTION See paragraph 2 below	
Applicant's or agent's file reference	
International application No. PCT/US04/42948	International filing date (day/month/year) 20 December 2004 (20.12.2004)
Priority date (day/month/year) 19 December 2003 (19.12.2003)	
International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 48/00 and US Cl.: 514/44	
Applicant UNIVERSITY OF CINCINNATI	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Date of completion of this opinion 08 September 2005 (08.09.2005)	Authorized officer Daniel M. Sullivan Telephone No. 703-308-0196
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/42948

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
- a. type of material
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 32

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 32 are so unclear that no meaningful opinion could be formed (*specify*):

The claim is improperly multiply dependent in that it depends from claims that are themselves multiply dependent (e.g., claims 30a and 31).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/42948

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1-31</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-31</u>	NO
Industrial applicability (IA)	Claims <u>1-31</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-31 lack novelty under PCT Article 33(2) as being anticipated by Szoka *et al.* US 5,661,025.

The claims 1-8 are directed to a method of delivering a biologically active molecule to a cell comprising contacting the cell with a biologically active molecule and a cellular delivery polymer; claims 9-11 are directed to a kit comprising at least one biologically active molecule and at least one cellular delivery polymer; claims 12-20 are directed to a complex comprising a cellular delivery polymer and an agent that is desirably taken up by cells, wherein the delivery polymer comprises a polycationic polymer structure; claims 22-29 are directed to various compositions of matter comprising the complex of claim 12; and claims 30 and 31 are directed to methods of treatment comprising administering the composition of claim 12.

Szoka *et al.* teaches a composition comprising a polynucleotide and a dendrimer polycation (see throughout, especially the discussion in columns 9 and 10). The composition of Szoka *et al.* meets the limitations of the claimed composition and the composition used in the claimed methods. Furthermore, the teachings of Szoka *et al.* anticipate the limitations of the dependent claims, which limit the cellular delivery polymer to a dendritic macromolecule, the biologically active molecule to a nucleic acid (*Id.*) or polypeptide (see especially the cell recognition components in the paragraph bridging column 13-14); and the nucleic acid to one of various types of nucleic acid (see especially column 90). Furthermore, Szoka *et al.* teaches that the composition disclosed therein can be used in methods of gene therapy according to the process claims (see especially the "field of the invention" section in column 1).

Claims 1-29 lack novelty under PCT Article 33(2) as being anticipated by Langer *et al.* 2002/0131951.

The limitations of the claims are discussed herein above. Langer *et al.* teaches a composition comprising a polynucleotide and a biodegradable poly(β -amino ester) (see throughout, especially the discussion in paragraphs 0008-0009). The composition of Langer *et al.* meets the limitations of the claimed composition and the composition used in the claimed methods. Furthermore, the teachings of Langer *et al.* anticipate the limitations of the dependent claims, which limit the cellular delivery polymer to a carbohydrate-containing biodegradable polyester, the biologically active molecule to a nucleic acid (*Id.*) or polypeptide (see especially targeting agents in paragraph 0105); and the nucleic acid to one of various types of nucleic acid (see especially the discussion in paragraphs 0081-0089). Furthermore, Langer *et al.* teaches that the composition disclosed therein can be used to deliver a biologically active molecule into a cell according to the process claims (see especially paragraph 0185).

Claims 1-31 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.